## REMARKS

Amendments to the claims have been made to respond to the issues and concerns raised in the Office Action, to clarify aspects in the specification and claims, and to refine claim language. The amendments are believed to be consistent with the disclosure originally filed. The amendments also have been particularly presented to avoid, where applicable, any admission or estoppel, generally, negatively affecting the scope of protection provided by the disclosure and claims of the present application, and also in a manner that avoids prosecution history estoppel, limitation of the scope of equivalences, or the like. The Applicant amends claims 124-141. Claims 1-123 and 142-143 have been cancelled. Thus, claims 124-141 remain in this application and are believed to be in a condition for allowance.

As a preliminary matter, the Applicant notes that many of the issues and concerns related to the present case present complex and intertwining considerations. Accordingly, in the event questions remain, the Applicant requests the opportunity to pursue an interview to resolve any issues or concerns.

The Office Action expressed certain nonstatutory double patenting concerns. While the Applicant disagrees that the pending claims raise a double patenting issue, the Applicant notes that it is willing to execute a terminal disclaimer so as to expedite prosecution of the current case and anticipates discussing the details regarding the same by way of an interview.

The Office Action raised obviousness concerns with respect to the Seidel (1997) reference. The Applicant disagrees with the concerns raised. Moreover, the Applicant notes that Seidel is both an inventor in the current case and a co-author of the reference. Unless a reference is a statutory bar, it may be removed and the rejection may be overcome by a showing that the reference was published by the Applicant himself. MPEP § 715.01(c); In re Facius, 408 F.2d 1396 (CCPA 1969). As a further showing, the Applicant submits as Exhibit A to these Remarks a copy of the Affidavit of co-inventor

George Seidel under 37 C.F.R. § 1.132, submitted in the parent case of the instant application. The Applicant believes that this document or a similar document referring to the instant application and the specific claims should be sufficient to remove Seidel (1997) as a reference. Moreover, combinations of references including Seidel (1997) do not establish a *prima facie* case of obviousness because Seidel (1997) must be removed and the remaining combinations of references do not disclose all the elements of the claimed invention as required by MPEP § 2143 and In re Royka, 490 F.2d 981 (CCPA 1974).

The Office Action raised various obviousness concerns with respect to the combination of Seidel (1996) and Brink. The Applicant respectfully disagrees with these concerns. To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP § 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *Id.* Second, there must be a reasonable expectation of success. *Id.* Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *Id.* Here, a *prima facie* case of obviousness has not been established because combining the Seidel (1996) and Brink references would provide no reasonable expectation of success. More particularly, as stated in the specification at page 22, lines 11-22, sperm transport is compromised in superovulated cattle, so animals were frequently artificially inseminated on multiple occasions and/or with multiple doses of semen. The specification goes on to state that the combination of low dose insemination with superovulation is surprising because superovulation was previously deemed to hinder such a combination. With respect to the Seidel (1996) and Brink references, neither reference suggests that the combination of low dose insemination with superovulation would work. Accordingly, combining the references would provide no reasonable expectation of success to counter the prevailing view at the time that superovulation would hinder such a combination.

The Office Action raises a number of indefiniteness concerns. Regarding the recitation of a "low number" of sperm cells, the Applicant disagrees with the

indefiniteness concern raised. However, to expedite examination of the current case, the Applicant has amended claims 124 and 128 to recite "having a number of sperm cells less than about one-half the number of sperm cells of a typical insemination dosage." The Applicant notes that the number of sperm cells in a typical insemination dosage is well within the ordinary skill in the art for common agricultural livestock animals. In bovine applications, for example, as discussed in the specification at page 19, lines 11-13, an absolute number of 500,000 sperm may be considered a low dose where currently 1 to 10 million sperm are provided. As can be seen, this absolute number is at least 50% or less of any value selected from the current range. For non-livestock animals, the Applicant notes that determining the number of sperm cells in a typical insemination dosage is merely a function of routine experimentation, as discussed below, and therefore is well within the ordinary skill in the art. Accordingly, the Applicant believes the indefiniteness concern has been fully addressed. The Applicant further notes the foregoing comments are equally applicable to the enablement concerns raised in the Office Action with respect to the predictability of low dose insemination.

Regarding the recitation of "success levels comparable to a typical insemination dosage", the Applicant disagrees with the indefiniteness concerns raised. However, to expedite examination of the current case, the Applicant has amended claim 124 to recite "success levels selected from the group consisting of at least 35%, at least 41%, at least 50%, and at least 90% of a typical insemination dosage". As discussed above, the number of sperm cells in a typical insemination dosage is well within the ordinary skill in the art. Accordingly, the Applicant believes the indefiniteness concern has been fully addressed.

Regarding the recitation of "between any of days 2 and 18," the Applicant disagrees with the indefiniteness concern raised. However, to expedite examination of the current case, the Applicant has amended claim 126 to include the recitation of "between any of days 2 and 18 of the estrus cycle." Accordingly, the Applicant believes the indefiniteness concern has been fully addressed.

Regarding the antecedent basis concern with respect to claims 127-129, the Applicant has amended claim 127 and believes this concern has been fully addressed.

Regarding the indefiniteness concern raised with respect to claims 136-141, the Applicant disagrees with the indefiniteness concern raised. However, the Applicant has amended claims 136-141 to remove the term "producing an animal of a desired sex". Accordingly, the Applicant believes the indefiniteness concern has been fully addressed.

The Office Action raises a number of enablement concerns. As to each of these, the Applicant disagrees that the pending claims are not enabled by the specification. However, to expedite examination of the application, the Applicant has amended all claims to recite a "female nonhuman mammal". As to any concerns which remain, it appears as best that can be determined that the Office is struggling with the level of experimentation necessary to apply the various separate details of the present case to any nonhuman mammal.

With respect to this point, the Applicant wishes to emphasize (as pointed out in the Office Action) that the test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. MPEP § 2164.01; United States v. Telectronics, Inc., 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). How a teaching is set forth, by specific example or broad terminology, is not important. MPEP § 2164.08; In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 370 (CCPA 1971). Claims are not rejected as broader than the enabling disclosure for non-inclusion of limitations dealing with factors which must be presumed to be within the level of ordinary skill in the art; the claims need not recite such factors where one of ordinary skill in the art to whom the specification and claims are directed would consider them obvious. MPEP § 2164.08; In re Skrivan, 427 F.2d 801, 806, 166 USPQ 85, 88 (CCPA 1970). In the present case, the Office Action expressly states that the specification provides one specific example in which a method for producing a nonhuman mammal using a low number of separated sperm while achieving success rates comparable to that

obtained with a typical insemination sample. As a result, the claims are in fact enabled for bovines with respect to the specific example provided by the specification. Moreover, the specification teaches the inventive principles which were applied in the specific example to enable a successful result in that case. It is these inventive principles that provide the correlation between the teachings of the specification and the scope of the claims and enable the claims for other non-human species.

As may be appreciated, the scope of enablement must only bear a reasonable correlation to the scope of the claims. MPEP § 2164.08; In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement is satisfied. MPEP 2164.01(b); In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). In the present case, the specific example teaches application of broader inventive principles. For example, the present case realizes the relationship of the sheath fluid to the success achieved in using low dose, separated sperm for artificial insemination:

> "While naturally it is possible to adjust either the pre- or post-sort fluids, in one embodiment the invention adjusts the sheath fluid (3) so that it imposes significantly less stress upon the cells than was previously accomplished. In one regard the invention is remarkable in that it removes the total focus from that of operation of the flow cytometer to a focus on handling and removing stress from the cells themselves." Specification at page 12, lines 7-11.
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> "For the sheath fluid, a substance is selected according to one embodiment of the invention so that it may be chemically coordinated to present minimal changes. Thus, by selecting the appropriate sheath fluid not only in context of flow cytometry parameters, but rather also in context of the cell parameters themselves, the changes experienced by the cells and the over all result of the sorting can be enhanced. This is shown conceptually in Figure 3. Figure 3 shows some type of chemical factor (such as citrate or other factors) as it may exist throughout the various phases of the process. For instance, the four phases shown might represent the following shown for a flow cytometry separation technique, but not to be so limiting: phase I may represent the existence of the cells within the cell source (1), phase II might show the existence of the cells as they are sorted in the sheath fluid environment, phase III might show the cells as they are collected after sorting and phase IV might show the reconstituted cells in a storage medium after sorting. These four phases as shown for the prior art may experience vastly different chemical factor environments. As shown conceptually, however, in the present invention the cells may experience very little change, most notably the dip or drop experienced between phases I and II may be virtually absent. This is as a result of the selection of the appropriate sheath fluid as mentioned above. Thus, as a result of being

subjected to an appropriate sheath fluid, the cells in the present invention may experience a much lower level of stress." Specification at page 12, lines 23-28, and page 13, lines 1-10.

Applying these principles to bovines, the specification at page 12, lines 19-20 notes that a citrate constancy metabolic composition may be very important and thus that a 2.9% sodium citrate solution is selected and coordinated for the sheath fluid, as taught by the specification at page 13, lines 18-20. More importantly, once it is realized that coordinating a sheath fluid may contribute to the successful use of low dose, separated sperm for artificial insemination, the particular parameters for specific species can be determined by routine experimentation.

As may be appreciated, the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. MPEP § 2164.01; In re Certain Limited-Charge Cell Culture Microcarriers, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), aff'd. sub nom. Massachusetts Institute of Technology v. A.B. Fortia, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). An extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance. MPEP § 2164.06; In re Colianni, 561 F.2d 220, 224, 195 USPQ 150, 153 (CCPA 1977). The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. MPEP § 2164.06; In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)). In the present case, the Applicant notes that considerable amounts of complex experimentation are routine for the field of animal reproduction technology. Attention is directed to the experimentation described in the patents and publications cited by the Applicant in the Information Disclosure Statements of the present case, which illustrate this point. Moreover, as discussed above, the teachings of the present case provide guidance for the direction along which experimentation should proceed with respect to other non-human species. As discussed above, for example, once it is recognized that chemically coordinating a sheath fluid is

important, the specific parameters for the sheath fluid may be determined by routine experimentation for any particular species. In fact, as described in the specification at page 12, lines 18-20, the teachings of the specification even provide two kinds of sheath fluids – citrate constancies and hepes buffered constancies – as starting points for experimentation.

The Applicant notes that the Office Action cites *Genentech Inc. v Novo Nordisk*, 42 U.S.P.Q.2d 1001 (Fed. Cir. 1997), for the proposition that it is the specification, not the knowledge of one skilled in that art, that must supply the novel aspects of the invention in order to constitute adequate enablement. As discussed above, the Applicant maintains that the specification of the present case in fact does teach novel aspects – it is the application of these novel aspects to specific non-human species that falls within the realm of routine experimentation. Moreover, this point is clarified by a review of *Genentech* itself. As discussed in *Genentech* at page 1010, the question before the court was whether the specification would have enabled a person having ordinary skill in the art at the time of filing to use cleavable fusion expression to make hGH without undue experimentation. However, as discussed in *Genentech* at page 1010, the specification at issue provided *no detail whatsoever* on how to make hGH using cleavable fusion expression. Nor were reaction conditions for the steps needed to produce hGH provided, and no description of any specific cleavable conjugate protein appeared. Further, as discussed in *Genentech* on page 1014, just prior to the sentence cited in the Office Action, there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill in the art when there is *no disclosure of any specific starting material or of any of the conditions* under which a process can be carried out. These conditions spelled out in *Genentech* are not the situation in the present case. As discussed above, for example with respect to the importance of chemically coordinating a sheath fluid, the conditions affecting the use of low dose, separated sperm in artificial insemination are described in the specification. Further, starting materials are even provided, as is the case for the citrate constancies and hepes buffered constancies discussed above. Consequently, the application of *Genentech* to the present case is not warranted.

Accordingly, for the reasons discussed above, the Applicant respectfully requests withdrawal of the enablement rejection raised in the Office Action.

The Office Action raises certain enablement concerns with respect to the Johnson (1997) reference. The Applicant respectfully disagrees with these concerns. The Applicant notes that the passage quoted in the Office Action discusses *direct application* of the technology for small numbers of sperm in cattle to swine. However, as discussed above, the low dose insemination technology for cattle taught by the examples of the present case are merely illustrative of the broader inventive principles taught by the current case. Accordingly, the specific protocols for cattle need not be made directly applicable to swine. Rather, such specific protocols for swine may be determined through routine experimentation based on the teachings of the broader inventive principles taught by the current case. The Applicant notes that the Johnson (1997) reference itself bears out this point. Specifically, immediately after the sentence quoted in the Office Action, the following is stated.

> "This is an area of research that could benefit greatly from more intensive research effort. Indeed, the whole swine artificial insemination industry would benefit from greater research emphasis, since the increasing use of AI will bring about increasing pressure for greater economy of spermatozoa per dose." Johnson (1997) reference, p. 262.

Accordingly, the Applicant respectfully submits that the Johnson (1997) reference raises no enablement concerns with respect to the current case.

The Office Action raises certain enablement concerns with respect to the Cran reference. The Applicant respectfully disagrees with these concerns and notes that the Cran reference itself at page 267 states that low pregnancy rates achieved were probably due to a combination of factors including the delay between semen collection and insemination, asynchrony between insemination and ovulation, semen dose, and the onset of seasonal anestrus. While the Office Action appears to concede these points, it nevertheless is stated no guidance is provided regarding how to modify the method of Cran. The Applicant respectfully submits that the deficiencies of Cran are well within

the ordinary skill in the art to address. Indeed, the statement of the problems themselves suggest their solution. More specifically, it appears the deficiencies of the Cran reference may be addressed by reducing the delay between semen collection and insemination, synchronizing insemination and ovulation, and inseminating at an earlier time prior to the onset of seasonal anestrus. With regard to semen dose, the Applicant respectfully submits that the current case teaches the use of low doses of sperm, as discussed elsewhere in these Remarks. Accordingly, the Applicant respectfully submits that the Cran reference raises no enablement concerns with respect to the current case.

The Office Action raises certain enablement concerns with respect to the Fugger reference. The Applicant respectfully disagrees with these concerns and notes that the teachings of Fugger relied on by the Office Action related to sperm shape and DNA difference are discussed in the context of human sperm. More particularly, the Fugger reference at page 1438 makes the point that it is *human* sperm cells that present unique characteristics that affect the ability to detect and separate X and Y sperm by flow cytometry. The Fugger reference goes on to distinguish the unique characteristics of human sperm, saying at page 1438 that most human sperm are heterogenous, vary substantially within and between individuals, are oval in shape, vary in the magnitude of difference in DNA content between X and Y chromosomes due to individual variation in size of the Y chromosome, and contain a relatively small 2.8% difference in total DNA content compared to >3.5% for most domestic animals. Importantly, the Applicant notes that all claims have been amended to recite a "nonhuman female mammal". Accordingly, the Applicant respectfully submits that the Fugger reference raises no enablement concerns with respect to the current case.

The Office Action raises certain enablement concerns with respect to the Johnson (1992) reference. The Applicant respectfully disagrees that the Johnson (1992) reference poses an enablement issue. Specifically, with respect to the difference in DNA content for turkeys and humans, the Applicant notes that all claims have been amended to recite a "nonhuman female mammal". Accordingly, the aspects of the Johnson (1992) reference with respect to turkeys and humans simply are not applicable to the current case. With

respect to the purity values for rabbit sperm, the Applicant notes that the sperm sorting described in the Johnson (1992) reference was accomplished with a flow cytometer. It is well known that the purity rates achieved by flow cytometers may be varied simply by adjusting the parameters of the flow cytometer. As just one example, reducing the sort rate of a flow cytometer predictably increases the accuracy of the sorting percentages achieved by the flow cytometer. Accordingly, the purity values for rabbit sperm stated in the Johnson (1992) reference cannot be taken as definitive, in as much as the values may have been dependent on the parameters used to operate the flow cytometer. For these reasons, the Applicant maintains that the Johnson (1992) reference cannot support an enablement rejection.

The Office Action raised certain informality concerns with respect to claims 126, 133, and 140. The Applicant has amended claims 126, 133, and 140 to address the informality concerns raised and believes these concerns have been fully addressed.

The Applicant, having addressed each of the concerns raised in the Office Action, respectfully requests reconsideration and withdrawal of the rejections and objections to the application. Allowance of claims 124-141 is requested at the Examiner's earliest convenience.

Dated this 30 day of March, 2005.

Respectfully submitted,

SANTANGELO LAW OFFICES, P.C.

By: _____

Misha Gregory Macaw
Attorney for the Applicant
PTO No. 55,417
125 South Howes, Third Floor
Fort Collins, Colorado 80521
(970) 224-3100